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(54) FLEXIBLE MULTIPLE COMPARTMENT DRUG CONTAINER

FLEXIBLER, MEHRERE ABTEILUNGEN AUFWEISENDER BEHÄLTER FÜR MEDIKAMENTE

RECIPIENT SOUPLE POUR MEDICAMENTS A COMPARTIMENTS MULTIPLES

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Description

[0001] The present invention relates to a flexible container for storage and combination of diluents and medicaments, and to a method of manufacturing the same. More particularly, the invention provides a single flexible container having multiple compartments to separately contain a diluent and a medicament for storage. The compartments are separated by frangible seals which may be ruptured by manipulation of the container to mix the contents and to deliver the contents through a port to a standard IV arrangement.

[0002] There exists an ongoing need for the development and improvement of containers for the administration of IV liquids in chemical or drug therapies, nutritional supplements and blood transfusions. Particularly, in the field of chemical and drug therapies, the IV solution delivered to the patient often comprises a mixed combination of a diluent and one or more medicaments. In many cases, the medicaments must be maintained separately from the diluent until immediately before use to prevent degradation. Common packaging of the diluent and medicaments is often further complicated by the character of the medicament which may be a powder sensitive to moisture contamination, or a powder or liquid sensitive to degradation under light or oxygen exposure.

[0003] Numerous recent improvements in the technology of IV containers have been made providing flexible containers which are less easily damaged and more easily stored and handled. Containers such as that disclosed in U.S. Patent Nos. 4,458,811 to Wilkinson and 4,608,043 to Larkin are representative of prior art multiple compartment flexible containers allowing separate storage of medicaments and diluents which may be mixed immediately prior to use. A second type of prior art devices provide a flexible diluent container with an attachment means for a second container containing a medicament and integral systems for engagement of the containers to maintain sterility while mixing the components.

[0004] Alternate systems in the prior art include combined containers wherein an inner container is physically manipulated from the exterior of a flexible covering container to release a medicament for mixing with a diluent in the flexible container. A vial contained within the flexible container having a plug or lid which may be extracted from the vial by manipulating the vial through the flexible walls of the container is exemplified in U.S. Patent No. 4,610,684 to Knox et al. An additional alternative is provided in the prior art by pre-mixing the medicament and diluent and freezing the container until ready for use to extend shelf life by preventing degradation of the pre-mixed solution. The complexities and disadvantages are self evident of numerous and complicated parts for the containers or the added requirement for refrigeration support devices of these prior art approaches.

[0005] US-A-4 629 080, which is considered to represent the closest prior art with respect to the present invention, discloses a flexible container for combined storage and administration of medicament and diluent for solutions, the container comprising: a flexible front sheet; a flexible rear sheet sealed to the front sheet at a common peripheral edge; a first peelable seal extending between two sides of the edge and separably joining the front and rear sheet to form a diluent compartment; a second peelable seal extending between the two sides and separably joining the front and rear sheet to form an outlet compartment and a medicament compartment intermediate the outlet compartment and the diluent compartment, the outlet compartment being empty when the diluent and medicament are in their separate compartments, wherein the first peelable seal is rupturable by hydraulic pressure generated by manipulation of the diluent compartment, the diluent and medicament are mixed by further manipulation of the container after rupture of the first peelable seal and the second peelable seal is rupturable by hydraulic pressure generated by further manipulation of the now joined diluent and medicament compartments, so that the diluent-medicament solution can flow into the outlet compartment; and an outlet port in communication with the outlet compartment.

[0006] US-A-4 602 910 describes a compartmented and collapsible container system for sterile components which has a storage compartment for each component with a secondary container compartment within a larger container compartment. The compartments are separated by a frangible seal to be opened by hydraulic pressure. The outlet port of the container includes a body portion which is sealed to the front and rear sheets within the common peripheral edge. There is no empty outlet compartment and the storage compartments are arranged within each other so that the hydraulic pressure applied for opening the seals between the compartments is not directed toward the outlet port. The arrangement of the compartments within each other, however, is difficult to manufacture.

[0007] Further improvement over the prior art containers is desireable in that sealing mechanisms between compartmented containers such as that disclosed in Wilkinson have been complex and costly. Similarly, interconnecting devices for combination of two containers or for mechanical puncturing and interconnection of joined containers require numerous components which are expensive to fabricate and increase the possibility of failure. In addition, the dispensing configuration of prior art containers may preclude complete emptying of the container or require the presence of significant quantities of air in the container to allow complete delivery of the fluid contents of the container. Presence of significant quantities of air in the sealed container may produce difficulties during sterilization of the containers since air expansion at the sterilization temperatures may damage the flexible material of the container. Finally, configuration of multi-compartmented prior art containers has, in many cases, precluded assurance of complete mixing of medicaments with diluents prior to delivery to the patient.

[0008] It is therefore desirable to provide an IV container having multiple compartments for storage of diluent and medicaments in a single package having simple frangible seals dividing the compartments which may be ruptured for combination and mixing of the contents. It is further desirable that the container arrangement preclude the inadvertent delivery of any of the components prior to mixing and allow visual verification of condition of the components prior to mixing and after mixing is complete, before dispensing. It is also desireable that the contents of the container be completely deliverable to the patient without the requirement for the presence of a significant quantity of air in the container. The capability for enhanced protection of the contents in one or more of the compartments of the container against moisture or oxygen permeation or light degradation is also desirable.

[0009] The present invention provides the desired features with a container designed according to claim 1, and with a method of manufacturing the container according to claim 14.

[0010] The flexible materials of the sheets forming the container are selected based on requirements of the contained diluents and medicaments. In a first embodiment, a front sheet is a transparent multi-layer laminate having an inner layer of low melting temperature polypropylene and an outer layer of a higher melting temperature polypropylene. The rear sheet is impermeable to water vapor and comprises a laminated material having an inner layer of polypropylene, a middle layer of aluminum foil and an outer layer of polyester film. Vapor impermeability of the rear sheet extends the shelf life of the product by reducing by half the permeation of diluent vapor from the container and permeation into the medicament, if a powder, of vapor from the atmosphere. If additional reduction in vapor permeability is required for the medicament compartment, a third sheet of laminated material which, in one embodiment, is identical to the rear sheet and sized to cover the medicament compartment may be affixed over the front sheet in the region of the medicament compartment to provide a vapor impermeable enclosure.

[0011] The frangible or peelable seals between the compartments in the container are formed using a hot bar technique sealingly adhering the interfacing polypropylene layers of the front and rear sheet. Attachment of the third sheet to the medicament compartment may be accomplished also using a hot bar technique adheringly sealing the inner polypropylene layer of third sheet to the outer polypropylene layer of the front sheet. The third sheet may subsequently be peelably removed at the time of use to expose the medicament for visual inspection prior to mixing.

[0012] An outlet port is mounted in the transparent front sheet in the region of the third compartment by inserting the port through an aperture in the sheet sized to receive the port with an overlapping engagement of a perimeter flange and the inner layer of the sheet which may then be heat sealed. Arrangement of the outlet port in the front sheet of the container allows collapse of the rear sheet of the container against the front sheet to fully drain the container and avoid any requirement for introduction of significant quantities of air into the container to allow complete dispensing.

[0013] These and other features, aspects and advantages of the present invention will be more fully understood when considered with regard to the following detailed description, appended claims and accompanying drawings (of a preferred embodiment) wherein:

FIG. 1 is a semi-schematic front view of one exemplary embodiment of a container provided in accordance with practice of the present invention showing the arrangement of the compartments and intervening seals including the outlet port;

FIG. 2 is a semi-schematic side cross section view taken along line 2-2 of FIG. 1 showing the flexible sheets forming the container and the orientation and configuration of the outlet port, thickness of the layers in the sheets is exaggerated for clarity;

FIG. 3 is a semi-schematic cutaway view along line 3-3 of FIG. 2 showing the laminate configuration of the flexible sheets employed in the container;

FIG. 4 is a semi-schematic pictorial view showing a peelable medicament compartment cover being removed for inspection of the medicament prior to mixing and use;

FIG. 5 is a semi-schematic pictorial cutaway demonstrating the manipulation of the container to separate the first peelable seal to mix the diluent and medicament; and

FIG. 6 is a semi-schematic pictorial cutaway demonstrating the manipulation of the container to separate the second peelable seal to dispense the medicated solution.

[0014] Referring to FIGs. 1 and 2, there is shown an exemplary embodiment of a container 10 provided in accordance with practice of principles of this invention. Although the container 10 can be viewed in any orientation, for purposes of explanation herein, the position of the components of the container relative to each other are described as positioned in FIGs. 1 and 2. The container 10 is formed from a front sheet 12 and a back or rear sheet 14 which may be laminates of flexible materials to be described in greater detail subsequently. The sheets forming the container are sealed together at their common peripheral edge forming an edge seal 16 which extends around the entire periphery of the container. Such peripheral seals may vary in configuration and width. A patterned seal such as that shown for the top seal 16a and the bottom seal 16b in FIG. 1 may be used to provide grasping areas for the user to handle the container and for the attachment to IV support stands.

[0015] The container 10 is partitioned into three separate compartments in the embodiment shown. An upper compartment 18, an intermediate compartment 20 and a lower compartment 22. A shown in FIG. 2, the upper and intermediate compartments are separated by a first peelable seal 24 and the intermediate and lower compartments are separated by a second peelable seal 26. The peelable seals extend between the two sides of the container, right side 10a and left side 10b, joining the front and rear sheets. A "peelable seal" as used herein is a seal which is sufficiently durable to allow normal handling of the container yet which will peel or separate substantially completely from the right side to the left side under pressure applied by manipulating the container thereby allowing mixing and dispensing of the container contents. A peelable seal is formed by a partial melting together of the polymer present in the adjacent layers of the front and back sheets. The seal is obtained by heat sealing with varying times, temperatures and pressures to be described in greater detail subsequently. Conversely, the peripheral edge seal 16 is significantly stronger than the "peelable seals" and will not be ruptured by pressures generated to separate the peelable seals. Configuration of the peelable seals as a straight line between the peripheral seals as opposed to a chevron design or the like, promotes substantially complete peeling of the entire seal during use of the container as will be described in greater detail subsequently.

[0016] In a typical application for the container 10 of the present invention, the upper compartment 18 is filled with a liquid diluent and the intermediate compartment 20 is filled with a medicament. The lower compartment 22 provides the interface for an outlet port 30 and remains empty until the container is used. The outlet port extends through an aperture 32 in the front sheet 12 of the container 10. A flange 34, best seen in FIG. 2, on the outlet port engages the inner surface of the front sheet around the periphery of the aperture which may be heat sealed to the flange forming an outlet seal 36. The outlet port 30 comprises a body portion 38 and a nozzle 40 which is attachable to a standard IV administration device. As best seen in FIG. 2, the configuration of the outlet port 30 allows the rear sheet 14 to collapse fully against the front sheet and flange 34 of the outlet port 30. Also, external air pressure on the front and rear sheets of the container tends to force the front and rear sheets of the container 10 together during dispensing of the contents. This combination of features allows the contents of the container to be fully dispensed with only a small quantity of the solution remaining in the ullage space 42 of the outlet port 30. In the embodiment shown, this ullage results from the molding process employed for forming the outlet port. Additional ullage may arise depending on configuration of the IV attachment or "spike" and positioning of a sterile sealing diaphragm typically located at the top of the cylindrical nozzle 40. Alternate forming methods leaving no ullage may be employed to allow complete draining of the container. The combination of outlet port configuration and general configuration of the container precludes a requirement for presence of substantial quantities of air within the container to allow complete draining of the solution to be administered.

[0017] The materials employed in the front and rear sheets of the container 10 are selected based on the material to be stored. Preferably, at least one of the sheets is transparent to allow the contents of the container to be visually inspected and to allow the level of the solution in the container to be seen during dispensing. Typically, the front sheet 12 is transparent. Suitable materials for fabrication of the front sheet are typically laminated, multi-layer films. Examples of such films are disclosed in U. S. Patent No. 4,803,102 to Raniere et al.

[0018] Referring particularly to FIG. 3, a laminate employed as the front sheet 12 in one exemplary embodiment of the container 10 comprises a transparent thermoplastic polymer laminate having an inner polymer seal layer 44 and an outer higher temperature polymer layer 46. Polypropylene or polyethylene or combinations of the two can be used as the polymer. In one embodiment, the inner or seal layer comprises a blend of about 80% polypropylene polyethylene copolymer available from Fina Oil and Chemical Company, Deerpark, TX having a commercial designation of Z9450 and 20% styrene butadiene elastomer rubber available from Shell Chemical Corporation under the trademark "Kraton" and having a commercial designation GI652. The outer high temperature layer 46 is a high ethylene content random copolymer available from Fina having a commercial designation 7450. In one embodiment, the inner layer 44 of the 80%/20% polypropylene copolymer and styrene butadiene elastomer is 0,18 mm (7 mils) thick while the outer layer 46 of the higher temperature polypropylene is 0,025 mm (1 mil) in thickness. Other thicknesses can be provided, as described.

[0019] For certain combinations of diluents and medicaments, the rear sheet 14 can have the same composition and configuration as the front sheet 12. Considerations of shelf life and susceptibility to vapor permeability into or out from the container 10 may require the use of an alternate material for the rear sheet. In the embodiment of the container shown in the drawings (FIG. 3), a rear sheet 14 is employed which is impermeable to water vapor to increase shelf life. The rear sheet comprises a three layer laminate including an aluminum foil. One such suitable laminate is a commercially available product from Reynolds Aluminum designated "Flex Can II RT" which includes an outer layer 48 of polyester, a middle layer 50 of aluminum foil and an inner seal layer 52 of polypropylene. The individual layers of the "Flex Can" laminate are adhesively bonded to each other using 1,13 kg (2.5 pounds) per ream adhesive between the outer layer and aluminum foil and a 0,45 kg (1.0 pound) per ream adhesive between the aluminum foil and inner polypropylene seal layer. Typical dimensions of the "Flex Can II" laminate are 12,2 µm (.48 mil) for the outer polyester layer, 17,8 µm (.7 mil) for the aluminium foil and 0,076 mm (3.0 mil) for the polypropylene layer.

[0020] Embodiments that have been fabricated indicate that preferable material choices for the front and rear sheets

to optimize the performance of the peelable seals incorporate an interfacing seal layer on one sheet comprising a blend incorporating a polymer and styrene butadiene elastomer blend for the interfacing layer and the opposing interfacing layer on the mating sheet comprising a polymer layer without the elastomer. Alternatively, the interfacing layers of the front and rear sheets comprise polymer and styrene butadiene elastomer blends having differing percentages of the styrene butadiene elastomer. Table I is a non-limiting list showing seven examples of single and multiple layer films or laminates useful in fabrication of various embodiments of the invention.

TABLE I

Description of film structures for front and rear sheets: Designator		
1. S62-71	Outside Layer:	25,4 µm (1 Mil) Fina 7450XAC PP/PE random copolymer
	Interface Layer:	0,18 mm (7 Mil) 20% Kraton/80% Fina Z9450 blend
2. S62-75	Single Layer:	Fina Z-9450
3. Z4660	Single Layer:	Horizon Z-4660 20% blend*
4. S62-100	Outside Layer:	30,5 µm (1.2 mil) ECDEL 9967** Copolyester
	Tie Layer:	20,3 µm (.8 mil) Kraton Gl652
	Interface Layer:	0,16 mm (6.2 mil) 30% Kraton/70% Fina Z9450 blend
5. S62-101	Outside Layer:	30,5 µm (1.2 mil) ECDEL 9967 Copolyester
	Tie Layer:	20,3 µm (.8 mil) Kraton Gl652
	Interface Layer:	0,16 mm (6.2 mil) 40% Kraton/60% Fina Z9450 blend
6. X62-053	Single Layer:	0,2 mm (8 mil) Fina 7450AC PP/PE Random Copolymer
7. Foil	Reynolds Flex Can II RT	

*Denotes a product of Horizon Polymers, a Division of Ferro Corporation, Houston, TX. Blend contains a thermoplastic elastomer other than styrene butadiene.
**"ECDEL" is a trademark of Eastman Chemical Co. of Kingsport, Tenn.

[0021] In certain applications, particularly where the medicament is a powder, additional protection for the second or intermediate compartment 20 of the container 10 to preclude vapor transmission and degradation of the powder is desired. Referring particularly to FIGs. 2 and 3, in the illustrated embodiment, a third sheet 54 is employed to cover the intermediate compartment 20. In an exemplary embodiment, the composition of the third or cover sheet is identical to the rear sheet 14 and comprises a laminate including aluminum foil. The use of the aluminum foil laminate further provides protection from degradation of the medicament due to light exposure. The aluminum layer in the third sheet 54 and rear sheet prevents penetration of UV and visible spectrum light into the intermediate compartment 20 of the container.

[0022] The third sheet 54 can be removed from the container prior to its use to allow examination of the powder medicament. In one embodiment, best seen in FIGs. 2 and 4, the third sheet 54 includes a tab 56 which may be grasped to peel the third sheet from the transparent front sheet 12 so that the contents of the intermediate compartment 10 can be visually inspected.

Manufacture of the Container

[0023] The composition of the front sheet 12, rear sheet 14 and third sheet 54, allow the creation of the peripheral seals and peelable seals using heat sealing techniques. Hot bars or dies are used at differing temperatures, pressures and application times to bring interfacing portions of the laminates employed to temperatures near or above melting to allow migration of material across the interface to form a bond of the desired strength and characteristics. For the bilayer film comprising the front sheet 12 and Reynolds foil laminate comprising the rear sheet 14, a procedure for fabrication of the container 10 of the illustrative embodiment comprises cutting the front sheet to the desired dimensions for the container and cutting the aperture 32 for the outlet port 30. The outlet port in the embodiment shown in the drawings is injection molded and has a composition of 40% Fina Z9450 polypropylene copolymer and 60% Shell Kraton G4652 styrene butadiene elastomer. The outlet port is inserted through the aperture in the front sheet 12 and a heated die is employed to create the seal 36 of the front sheet adjacent the aperture to the flange 34 of the outlet port. A die temperature of 204°C (400° F) with a dwell time of 1.5 seconds under a pressure of $1,2 \times 10^6$ N/m^2 (170 pounds per square

inch) is used to accomplish the seal for the bilayer film and outlet port combination described previously. The third sheet 54 comprising the overlay for the intermediate compartment 20 is cut to size, positioned over the area to become the medicament compartment and attached to the front sheet 12 forming seals 25 and 27 using a die heated to 143°C (290° F) with a dwell time of 3.0 seconds under 0,5 x 10^6 N/m^2 (70 PSI) of pressure. The rear sheet 14 is cut to size and mated to the front sheet with the seal 16 around the peripheral edge created by a hot die at 166°C (330° F) with a dwell time of 25 seconds under 1,3 x 10^6 N/m^2 (164 PSI) of pressure.

[0024] The peelable seals 24 and 26 dividing the compartments in the container 10 are then created using double hot bars comprising a front bar in alignment with a rear bar constraining the elements of the container therebetween to form the seal thereby providing a substantially uniform seal across the container. The front bar contacting the previously combined third sheet 54 and front sheet 12 is maintained at a temperature of 130°C (265° F). The rear bar contacting the rear sheet 14 has a thin rubber covering to assure uniform application of pressure, and is maintained at 124°C (255° F). The double bars are maintained in contact with the front and rear sheets for 2 seconds with a pressure of 0,9 x 10^6 N/m^2 (130 PSI). The peelable seals 24 and 26 as shown in FIG. 2 may be made individually with a single double bar set up or simultaneously with a twin double bar set up.

[0025] Without being bound by theory, it is thought that the peelability of the seals is obtained by limiting the time, pressure and temperature to that necessary to fuse the interface between the inner layers of the front and rear sheets which have a lower melting temperature than the intermediate and outer layers. The depth of the structural alteration in the inner layers in the fusion zone is limited, thereby imparting the peelable character to the seal while providing sufficient strength to prevent breakage in normal handling of the container. Higher temperatures and associated pressures and times are used for the peripheral seals and outlet seal, producing structure altering effects in a greater portion or depth of the sealing layers. Those skilled in the art will recognize various techniques for alternating the order of accomplishing the various seals and the orientation of the container 10 to allow filling the compartments with appropriate diluents and medicaments.

[0026] Preferred sealing parameters for several of the materials provided in various embodiments of the invention discussed previously with respect to Table I are shown in Table II.

TABLE II

Sealing parameters for laminate combinations			
Front Sheet (12)	S62-71	S62-71	S62-71
Rear Sheet (14)	S62-101	Foil	X62-053
Medicament cover (54)	Foil	Foil	Foil
Edge Seal (16)			
Temp.°C (F)	190 (375)	166 (330)	157 (315)
Time (Sec)	31	25	22.5
Pressure x 10^6 N/m^2 (psi)	1,5 (218)	1,3 (164)	1,5 (218)
Peelable Seals (24, 26)			
Front bar°C (F)	132 (270)	130 (265)	132 (270)
Rear bar°C (F)	132 (270)	124 (255)	127 (260)
Time (sec)	2	2	7
Pressure x 10^6 N/m^2 (psi)	0,9 (130)	0,9 (130)	0,9 (130)
Medicament Cover Seals (25,27)			
Temp.°C (F)	143 (290)	143 (290)	143 (290)
Time (sec)	3	3	3
Pressure x 10^6 N/m^2 (psi)	0,5 (70)	0,5 (70)	0,5 (70)

[0027] Incorporating the sealing techniques described previously, filling of the container may be accomplished using several techniques. In an exemplary process employing the bi-layer film and Reynolds multi-layer foil laminate, a portion of the periphery comprising one side of the intermediate compartment 20 and a portion of one side of the upper compartment 18 are left unsealed for filling. The upper compartment 18 is then filled with liquid diluent through the opening.

The unsealed portion of the periphery adjacent the compartment is then sealed using a hot die, e.g. at 130°C (265° F) with a dwell time of 5 seconds under 2.76×10^6 N/m^2 (400 PSI) pressure. The container is then autoclaved for sterilization. The intermediate compartment 20 is then dried and filled with a powder medicament and the edge adjacent the compartment 20 is then sealed using a hot die.

[0028] The production process further includes installing a moisture and light impermeable foil covering the medicament compartment, wherein at least a portion of the foil is removable for visual inspection of the medicament in the medicament compartment.

[0029] A production process for fabrication and filling of the container is anticipated to include the steps of fabrication of the outlet port and multi-layered laminate sheets, insertion and sealing of the outlet port 30 to the front sheet, fabrication of the container and seals employing a form, fill and seal process with filling of the diluent while leaving the intermediate powder compartment open, steam sterilization of the container 10 followed by aseptically drying, filling and sealing the powder compartment. Quality control inspection of the container and packaging for storage and shipment could then be accomplished.

Use of the Container

[0030] Use of the completed container is independent of the production technique employed. The triple compartmented container 10 and mixing system will be received by health care personnel in the completed configuration shown in FIGs. 1 and 2. Referring now to FIG. 4, in preparing to use the container, the medicament may be inspected by grasping the tab 56 on the third sheet 54 and peeling the third sheet from the container 10 to enable visualization of the intermediate compartment 20 containing the powdered medicament. If the medicament appears dry and in normal condition, the solution can be mixed as shown in FIG. 5 by manipulating the container to compress the front and rear sheets in the area of the upper compartment 18. The pressure from the hydraulic forces created by manipulation of the container, ruptures the peelable seal between the upper and intermediate compartment (shown in the ruptured condition as 24'). Further manipulation by shaking causes mixing of the liquid diluent and the powdered medicament. Verification that complete mixing is obtained is made by visually observing the mixed solution. After complete mixing is accomplished, the peelable seal between the intermediate and lower compartment is broken as shown in FIG. 6 by again compressing the front and rear sheets of the container creating hydraulic pressure in the container to rupture the seal (shown in the ruptured condition as 26'). The solution is then dispensed from the container through the outlet port 30 using a standard IV delivery device 60.

[0031] The arrangement of the container 10 precludes delivery of unmixed diluent through the outlet port 30. Further, the arrangement of the intermediate compartment 20 between the diluent and outlet port enhances the probability of complete mixing and delivery of the medicament to the patient. For containers including a liquid diluent and powder medicament, rupture of the first peelable seal between the upper compartment 18 and intermediate compartment 20 is essentially assured prior to rupture of the second peelable seal between the intermediate compartment 20 and lower compartment 22 since the hydraulic forces developed in the diluent by manipulating the container cannot be transmitted through the powder in the intermediate compartment until the first seal has been ruptured and mixing of the diluent and powder has commenced. For those cases where a liquid medicament may be used, the relative size between the diluent compartment and the medicament compartment and the placement of the smaller compartment intermediate the larger compartment and the lower or outlet compartment assures development of hydraulic forces which will rupture the seal between the diluent and medicament compartments before rupture of the second seal with minimal care.

[0032] Those skilled in the art will recognize that the primary discussion of embodiments employing a liquid diluent and a single powdered medicament do not limit the scope of the invention. Use of liquid medicaments in an intermediate compartment or a plurality of compartments for powdered and liquid medicaments to be mixed with the diluent may be employed using the present invention.

[0033] Having now described in detail the invention as required by the patent statutes, those skilled in the art will recognize minor modifications or alterations to accomplish the specific applications. Such modifications and alterations are included within the scope and intent of the invention as described in the following claims.

Claims

1. A flexible container (10) for combined storage and administration of medicament and diluent for solutions, the container (10) comprising:

   a transparent flexible front sheet (12);

   a flexible rear sheet (14) sealed to the front sheet (12) at a common peripheral edge (16);

a first peelable seal (24) extending between two sides of the edge (16) and separably joining the front and rear sheet (12, 14) to form a diluent compartment (18);

a second peelable seal (26) extending between the two sides and separably joining the front and rear sheet (12, 14) to form an outlet compartment (22) and a medicament compartment (20) intermediate the outlet compartment (22) and the diluent compartment (18), the outlet compartment (22) being empty when the diluent and medicament are in their separate compartments (18, 20), a moisture impermeable cover sheet being sealed to the front sheet, said cover sheet being sized to extend over the medicament compartment (20) and being removable therefrom, wherein the first peelable seal (24) is rupturable by hydraulic pressure generated by manipulation of the diluent compartment (18), the diluent and medicament are mixed by further manipulation of the container (10) after rupture of the first peelable seal (24) and the second peelable seal (26) is rupturable by hydraulic pressure generated by further manipulation of the now joined diluent and medicament compartments, so that the diluent/medicament solution can flow into the outlet compartment (22); and

an outlet port (30) in communication with the outlet compartment (22), the outlet port (30) being adapted for connection to an IV administration device, whereby the diluent/medicament solution is administered to a patient.

2. A flexible container as defined in claim 1 wherein the flexible rear sheet (14) is vapor impermeable.

3. A flexible container as defined in claim 1 or 2 wherein the front sheet (12) comprises a transparent thermoplastic polymer.

4. A flexible container as defined in any one of claims 1 to 3 wherein the surface of the front sheet (12) adjoining the rear sheet (14) comprises a blend of thermoplastic elastomer and polymer; and the surface of the rear sheet (14) adjoining the front sheet (12) comprises a polymer selected from the group consisting of polypropylene, polyethylene and a polypropylene-polyethylene copolymer.

5. A flexible container as defined in any one of claims 1 to 4 wherein the rear sheet (14) comprises:

a multi-layer laminate having

an inner layer (52) comprising a polypropylene-polyethylene copolymer interfacing with the front sheet (12);

an intermediate layer (50) of aluminum foil; and

an outer layer (48) of polyester.

6. A flexible container as defined in any one of claims 1 to 5 wherein the front sheet (12) comprises:

a bi-layer laminate having

an inner layer (44) of a polypropylene-polyethylene copolymer blended with styrene butadiene elastomer in about an 80%/20% ratio interfacing the rear sheet (14); and

an outer layer (46) comprising polypropylene.

7. A container as defined in claim 6 wherein the polypropylene outer layer (46) of the front sheet (12) has a higher melting temperature than the inner layer (44) of the front sheet (12).

8. A flexible container as defined in claim 3 wherein the interfacing layers of the front and rear sheets (12, 14) each comprise a thermoplastic elastomer.

9. A flexible container as defined in claim 3 wherein the interfacing layers of the front and rear sheets (12,14) each comprise a polymer blended with styrene butadiene elastomer, the blend having a different percentage of styrene butadiene elastomer in the front and rear sheets.

10. A flexible container as defined in any one of claims 1 to 9 wherein the flexible front sheet (12) is transparent, and a moisture and light impermeable foil (54) covering the medicament compartment (20), wherein at least a portion of the foil (54) is removable for visual inspection of the medicament in the medicament compartment (20).

11. A flexible container as defined in claim 11 wherein the cover sheet (54) is a multilayer laminate comprising:

a polymer layer adjacent the front sheet;
an intermediate layer of aluminum foil; and
an outer layer of polyester.

12. A flexible container as defined in claim 10 or 11 wherein the flexible rear sheet comprises a multi-layer laminate including a layer of aluminum foil.

13. A flexible container as defined in any one of claims 1 to 12 wherein the medicament is a dry powder.

14. A method for forming a flexible container (10) for combined storage and administration of medicament and diluent for solutions, the method comprising the steps of :

providing a flexible, transparent, front sheet (12);

providing a flexible, vapor impermeable, rear sheet (14);

sealing the front and rear sheets (12,14) together at a common peripheral edge (16), wherein the surface of the front sheet (12) adjoining the rear sheet (14) comprises a blend of thermoplastic elastomer and polymer and the surface of the rear sheet (14) adjoining the front sheet (12) comprises a polymer selected from the group consisting of polypropylene, polyethylene and a polypropylene-polyethylene copolymer;

heating the front and rear sheets (12,14) in a first localized area to fuse together the heated portions of the adjoining surfaces, thereby forming a first peelable seal (24) extending between two sides of the common peripheral edge (16), said first peelable separably joining the front and rear sheets to thereby form a first compartment (18) for containing a diluent;

heating the front and rear sheets in a second localized area to fuse together the heated portions of the adjoining surfaces, thereby forming a second peelable seal (26) extending between the two sides of the common peripheral edge (16), said second peelabel seal (26) separably joining the front and rear sheets to thereby form an outlet compartment (22) and a compartment (20) for containing a medicament, the medicament compartment (20) being between the outlet compartment (22) and the diluent compartment (18);

filling the diluent compartment (18) with a diluent solution and filling the medicament compartment (20) with a medicament, while leaving the outlet compartment (22) empty;

installing a moisture and light impermeable foil (54) covering the medicament compartment (20), wherein at least a portion of the foil (54) is removable for visual inspection of the medicament in the medicament compartment (20);

wherein the first peelable seal (24) is rupturable by hydraulic pressure generated by manipulation of the diluent compartment (18), and wherein after rupture of the first peelable seal (24), the diluent and medicament are mixed together by further manipulation of the container to form a diluent/medicament solution and thereafter the second peelable seal (26) is rupturable by hydraulic pressure generated by further manipulation of the now joined diluent and medicament compartments so that the diluent/medicament solution can flow into the outlet compartment (22); and

forming an outlet port (30) in communication with the outlet compartment (22); the outlet port (30) being adapted for connection to an IV administration device.

15. The method according to claim 14 comprising heating the front and rear sheets (12,14) using a dual hot bar heat sealing apparatus having a front bar and a rear bar wherein the front bar temperature is higher than the rear bar temperature.

16. A flexible container as defined in any one of claims 1 to 13 wherein the outlet port (30) engages the front sheet (12) and comprises a body portion (38) connected to an aperture (32) of the front sheet (12) and extends transversely to the plane of the front sheet (12) whereby the rear sheet (14) can collapse against the front sheet (12) as the container is emptied.

17. The method as defined in any one of claims 14 to 16 wherein the outlet port (30) engages the front sheet (12) and comprises a body portion (38) connected to an aperture (32) of the front sheet (12) and extending transversely to the plane of the front sheet (12) whereby the rear sheet (14) is configured to collapse against the front sheet (12) as the diluent/medicament solution empties from the container.

Patentansprüche

1. Flexibler Behälter (10) zum kombinierten Aufbewahren und Verabreichen von Medikament- und Lösemittel für Lösungen, wobei der Behälter (10) aufweist:

   eine durchsichtige flexible vorderseitige Folie (12);

   eine flexible rückseitige Folie (14), die mit der vorderseitigen Folie (12) an einer gemeinsamen Umfangskante (16) verschweißt ist;

   eine erste ablösbare Naht (24), die sich zwischen zwei Seiten der Kante (16) erstreckt und trennbar die vorderseitigen und rückseitigen Folien (12, 14) verbindet, um ein Lösungsmittelabteil (18) zu bilden;

   eine zweite ablösbare Naht (26), die sich zwischen den beiden Seiten erstreckt und trennbar die vorderseitigen und rückseitigen Folien (12, 14) verbindet, um ein Auslaßabteil (22) und ein Medikamentenabteil (20) zwischen dem Auslaßabteil (22) und dem Lösungsmittelabteil (18) zu bilden, wobei das Auslaßabteil (22) leer ist, wenn sich Lösungsmittel und Medikament in ihren getrennten Abteilen (18, 20) befinden, eine feuchtigkeitsundurchlässige Abdeckfolie, die mit der vorderseitigen Folie verschweißt ist, wobei die Abdeckfolie derart bemessen ist, um sich über das Medikamentenabteil (20) zu erstrecken und davon entfernbar ist, wobei die erste ablösbare Naht (24) aufbrechbar ist durch hydraulischen Druck, der erzeugt wird durch Manipulation des Lösungsmittelabteils (18), das Lösungsmittel und das Medikament durch weitere Manipultion des Behälters (10) nach Aufbrechen der erste ablösbaren Naht (24) gemischt werden und die zweite ablösbare Naht (26) durch hydraulischen Druck aufbrechbar ist, der durch weitere Manipulation der nun verbundenen Lösungsmittel - und Medikamentabteile erzeugt wird, so daß die Lösungsmittel/Medikamentlösung nun in das Auslaßabteil (22) fließen kann; und

   einen Auslaßanschluß (30), der in Verbindung steht mit dem Auslaßabteil (22), wobei der Auslaßanschluß (30) an eine Verbindung zu einer IV-Verabreichungsvorrichtung angepaßt ist, durch welche die Lösungsmittel/Medikamentlösung einem Patienten verabreicht wird.

2. Flexibler Behälter in Anspruch 1, bei dem die flexible rückseitige Folie (14) dampfundurchlässig ist.

3. Flexibler Behälter in Anspruch 1 oder 2, bei dem die vorderseitige Folie (12) ein durchsichtiges thermoplastisches Polymer aufweist.

4. Flexibler Behälter nach einem der Ansprüche 1 bis 3, bei dem die der rückseitigen Folie (14) benachbarte vorderseitige Folie (12) eine Mischung aus thermoplastischem Elastomer und Polymer aufweist; und die Oberfläche der der vorderseitigen Folie (12) benachbarten rückseitigen Folie (14) ein Polymer aufweist, welches aus der Gruppe ausgewählt wurde, die aus Polypropylen, Polyethylen oder einem Polypropylen-Polyethylencopolymer gebildet wird.

5. Flexibler Behälter nach einem der Ansprüche 1 bis 4, bei dem die rückseitige Folie (14) aufweist:

   ein mehrschichtiges Laminat mit

   einer inneren Schicht (52), die ein Polypropylen-Polyethylencopolymer aufweist, welches mit der vorderseitigen Folie (12) in Verbindung steht;

einer Zwischenschicht (15) aus Aluminiumfolie; und

einer äußeren Schicht (48) aus Polyester.

6. Flexibler Behälter nach einem der Ansprüche 1-5, bei dem die vorderseitige Folie (12) aufweist:

ein zweischichtiges Laminat mit

einer inneren Schicht (44) aus einem Polypropylen-Polyethylencopolymer, welches mit einem Styrenbutadienelastomer in einem ungefähr 80%/20% Behältnis verblendet ist, die mit der rückseitigen Folie (14) in Verbindung steht; und

einer Außenschicht (46), die ein Polypropylen aufweist.

7. Behälter nach Anspruch 6, bei dem die Polypropylen-Außenschicht (46) der vorderseitigen Folie (12) eine höhere Schmelztemperatur als die Innenschicht (44) der vorderseitigen Folie (12) aufweist.

8. Flexibler Behälter nach Anspruch 3, bei dem die miteinander verbundenen Schichten der vorderseitigen und rückseitigen Folien (12, 14) jeweils ein thermoplastisches Elastomer aufweisen.

9. Flexibler Behälter nach Anspruch 3, bei dem die miteinander verbundenen Schichten der vorderseitigen und rückseitigen Folien (12, 14) jeweils ein Polymer aufweisen, welches mit Styrenbutadienelastomer verblendet ist, wobei der Blend einen unterschiedlichen Prozentsatz von Styrenbutadienelastomer in den vorderseitigen und rückseitigen Folien aufweist.

10. Flexibler Behälter nach einem der Ansprüche 1 bis 9, bei dem die flexible vorderseitige Folie (12) durchsichtig ist, und eine dampf- und lichtundurchlässige Folie (54) das Medikamentenabteil (20) abdeckt, wobei zumindest ein Teil der Folien (54) entfernbar ist für visuelle Inspektion des Medikaments im Medikamentenabteil (20).

11. Flexibler Behälter nach Anspruch 11, bei dem die Abdeckfolie (54) ein Mehrschichtlaminat ist mit:

einer Polymerschicht benachbart der vorderseitigen Folie;

einer Zwischenschicht aus Aluminiumfolie;

einer Außenschicht aus Polyester.

12. Ein flexibler Behälter nach Anspruch 10 oder 11, bei dem die flexible rückseitige Folie ein Mehrschichtlaminat mit einer Schicht aus Aluminiumfolie aufweist.

13. Flexibler Behälter nach einem der Anspruch 1 bis 12, bei dem das Medikament ein trockenes Pulver ist.

14. Verfahren zum Herstellen eines flexiblen Behälters (10) zum kombinierten Lagern und Verabreichen von Medikament und Lösung für Lösungen, welches Verfahren die folgenden Schritte aufweist:

Bereitstellen einer flexiblen, durchsichtigen vorderseitigen Folie (12);

Bereitstellen einer flexiblen, dampfundurchlässigen rückseitigen Folie (14);

Verschweißen der vorderseitigen und rückseitigen Folien (12, 14) miteinander an einer gemeinsamen Umfangskante (16), wobei die Oberfläche der vorderseitigen Folie (12), die der rückseitigen Folie (14) benachbart ist, ein Blend aus thermoplastischem Elastomer und Polymer und die Oberfläche der rückseitigen Folie (14), die der vorderseitigen Folie (12) benachbart ist, ein Polymer aufweist, welches aus der Gruppe ausgewählt ist, die aus Polypropylen, Polyethylen und Polypropylen-Polyethylencopolymer besteht;

Erhitzen der vorderseitigen und rückseitigen Folien (12, 14) in einem ersten begrenzten Bereich, um die erhitzten Abschnitte der benachbarten Oberflächen zu verschweißen, wodurch eine erste ablösbare Naht (24) gebildet wird, die sich zwischen zwei Seiten der gemeinsamen Umfangskante (16) erstreckt, wobei die erste

ablösbare Naht trennbar die vorderseitigen und rückseitigen Folien miteinander verbindet, um dabei ein erstes Abteil (18) zum Aufnehmen von Lösung zu bilden;

Erhitzen der vorderseitigen und rückseitigen Folien in einem zweiten begrenzten Bereich, um die erhitzten Abschnitte der benachbarten Oberflächen zusammenzuschweißen, wodurch eine zweite ablösbare Naht (26) gebildet wird, die sich zwischen den beiden Seiten der gemeinsamen Umfangskante (16) erstreckt, welche zweite lösbare Naht (26) trennbar die vorderseitigen und rückseitigen Folien miteinander verbindet, um dabei ein Auslaßabteil (22) und ein Abteil (20) zum Aufnehmen eines Medikaments zu bilden, wobei das Medikamentabteil (20) sich zwischen dem Auslaßabteil (22) und dem Lösungsabteil (18) befindet;

Füllen des Lösungsabteils (18) mit einer Lösungsmittellösung und Füllen des Medikamentabteils (20) mit einem Medikament, während das Auslaßabteil (22) leer bleibt;

Anbringen einer dampf- und lichtundurchlässigen Folie (54), die das Medikamentabteil (22) abdeckt, wobei zumindest ein Teil der Folie (54) entfernbar ist, für visuelle Inspektion des Medikaments im Medikamentabteil (20);

bei dem die erste ablösbare Naht (24) auftrennbar durch hydraulischen Druck ist, der durch Manipulation des Lösungsmittelabteils (18) erzeugt wird und bei dem nach Aufbrechen der ersten ablösbaren Naht (24) das Lösungsmittel und das Medikament miteinander vermischt werden durch weiteres Manipulieren des Behälters, um eine Lösungsmittel/Medikamentlösung zu bilden und danach die zweite ablösbare Naht (26) aufbrechbar ist durch hydraulischen Druck, der durch weiteres Manipulieren der nunmehr miteinander verbundenen Lösungsmittel- und Medikamentabteile erzeugt wird, so daß die Lösungsmittel/Medikamentlösung nun in das Auslaßabteil (22) fließen kann;

bilden eines Auslaßanschlusses (30) in Verbindung mit dem Auslaßabteil (22); wobei der Auslaßanschluß (30) an das Verbinden an eine IV-Verabreichungsvorrichtung angepaßt ist.

15. Verfahren nach Anspruch 14 umfassend das Erhitzen der vorderseitigen und rückseitigen Folien (12, 14) unter Verwendung eines Doppelbacken-Thermoschweißapparates, der einen vorderen Backen und einen hinteren Backen aufweist, wobei die Temperatur des vorderen Backens höher ist als die Temperatur des hinteren Backens.

16. Flexibler Behälter nach einem der Ansprüche 1 bis 13, bei dem sich der Auslaßanschluß (30) mit vorderseitigen Folien (12) in Eingriff befindet und einen Körperabschnitt (38) aufweist, der mit einer Öffnung (32) der vorderseitigen Folie (12) verbunden ist und sich quer zur Ebene der vorderseitigen Folie (12) erstreckt, wobei die rückseitige Folie (14) vollständig gegen die vorderseitige Folie (12) zusammenfällt, wenn der Behälter geleert wird.

17. Das Verfahren nach einem der Ansprüche 14 bis 16, wobei der Auslaßanschluß (30) sich mit der vorderseitigen Folie (12) in Eingriff befindet und einen Körperabschnitt (38) aufweist, der mit einer Öffnung (32) in der vorderseitigen Folie (12) verbunden ist und sich quer zu der Ebene der vorderseitigen Folie (12) erstreckt, wobei die rückseitige Folie (14) derart gestaltet ist, um vollständig gegen die vorderseitige Schicht (12) zusammenzufalen, wenn die Lösungsmittel/Medikamentlösung aus dem Behälter entleert wird.

Revendications

1. Récipient flexible (10) pour le stockage et l'administration combinés de médicament et de diluant pour des solutions, le récipient (10) comprenant :

   - une feuille frontale flexible transparente (12) ;
   - une feuille arrière flexible (14) scellée sur la feuille frontale (12) au niveau d'un bord périphérique commun (16) ;
   - un premier joint décollable (24) s'étendant entre deux côtés du bord (16) et joignant séparément la feuille frontale et la feuille arrière (12, 14) pour former un compartiment (18) pour diluant ;
   - un second joint décollable (26) s'étendant entre les deux côtés et joignant séparément la feuille frontale et la feuille arrière (12, 14) pour former un compartiment de sortie (22) et un compartiment (20) pour médicaments entre le compartiment de sortie (22) et le compartiment (18) pour diluant, le compartiment de sortie (22) étant vide lorsque le diluant et le médicament sont dans leurs compartiments distincts (18, 20), une feuille de couverture imperméable à l'humidité étant scellée sur la feuille frontale, ladite feuille de couverture étant dimen-

sionnée pour s'étendre par-dessus le compartiment (20) pour médicaments et pouvant être enlevée dudit compartiment, où le premier joint décollable (24) peut être rompu par pression hydraulique générée par manipulation du compartiment (18) pour diluant, le diluant et le médicament étant mélangés par une autre manipulation du récipient (10) après rupture du premier joint décollable (24), le second joint décollable (26) pouvant être rompu par la pression hydraulique générée par une autre manipulation des compartiments pour diluant et médicaments à présent joints, de sorte que la solution diluant/médicament peut s'écouler dans le compartiment de sortie (22) ; et

- un orifice de sortie (30) communiquant avec le compartiment de sortie (22), l'orifice de sortie (30) étant adapté pour être relié à un dispositif d'administration par voie intraveineuse, où la solution diluant/médicament est administrée à un patient.

2. Récipient flexible comme défini dans la revendication 1, dans lequel la feuille arrière flexible (14) est imperméable à la vapeur.

3. Récipient flexible comme défini dans la revendication 1 ou 2, dans lequel la feuille frontale (12) comprend un polymère thermoplastique transparent.

4. Récipient flexible comme défini dans l'une quelconque des revendications 1 à 3, dans lequel la surface de la feuille frontale (12) adjacente à la feuille arrière (14) comprend un mélange d'élastomère et de polymère thermoplastiques, la surface de la feuille arrière (14) adjacente à la feuille frontale (12) comprenant un polymère sélectionné dans le groupe se composant de polypropylène, de polyéthylène et un copolymère de polypropylène-polyéthylène.

5. Récipient flexible comme défini dans l'une quelconque des revendications 1 à 4, dans lequel la feuille arrière (14) comprend :

- un laminé multicouche ayant

  -- une couche intérieure (52) comprenant un copolymère de polypropylène-polyéthylène en contact interfacial avec la feuille frontale (12) ;
  -- une couche intermédiaire (50) constituée d'une feuille d'aluminium ; et
  -- une couche extérieure (48) en polyester.

6. Récipient flexible comme défini dans l'une quelconque des revendications 1 à 5, dans lequel la feuille frontale (12) comprend :

- un laminé bicouche ayant

  -- une couche intérieure (44) d'un copolymère de polypropylène-polyéthylène mélangé avec un élastomère de butadiène-styrène suivant un rapport de 80 %/20 % environ, ladite couche intérieure étant en contact interfacial avec la feuille arrière (14) ; et
  -- une couche extérieure (46) comprenant du polypropylène.

7. Récipient flexible comme défini dans la revendication 6, dans lequel la couche extérieure (46) en polypropylène de la feuille frontale (12) a une température de fusion supérieure à celle de la couche intérieure (44) de la feuille frontale (12).

8. Récipient flexible comme défini dans la revendication 3, dans lequel les couches interfaciales des feuilles frontale et arrière (12, 14) comprennent chacune un élastomère thermoplastique.

9. Récipient flexible comme défini dans la revendication 3, dans lequel les couches interfaciales des feuilles frontale et arrière (12, 14) comprennent chacune un polymère mélangé avec un élastomère de butadiène-styrène, le mélange ayant un pourcentage différent d'élastomère de butadiène-styrène dans les feuilles frontale et arrière.

10. Récipient flexible comme défini dans l'une quelconque des revendications 1 à 9, dans lequel la feuille frontale flexible (12) est transparente, et comprenant une feuille (54) imperméable à l'humidité et ne laissant pas passer la lumière, recouvrant le compartiment (20) pour médicaments, où au moins une partie de la feuille (54) peut être enlevée pour le contrôle visuel du médicament dans le compartiment (20) pour médicaments.

11. Récipient flexible comme défini dans la revendication 11, dans lequel la feuille de couverture (54) est un laminé multicouche comprenant :

- une couche de polymère adjacente à la feuille frontale ;
- une feuille intermédiaire constituée d'une feuille d'aluminium ; et
- une couche extérieure en polyester.

12. Récipient flexible comme défini dans la revendication 10 ou 11, dans lequel la feuille arrière flexible comprend un laminé multicouche comprenant une couche constituée d'une feuille d'aluminium.

13. Récipient flexible comme défini dans l'une quelconque des revendications 1 à 12, dans lequel le médicament est une poudre sèche.

14. Procédé pour former un récipient flexible (10) pour le stockage et l'administration combinés de médicament et de diluant pour solutions, le procédé comprenant les étapes consistant :

- à réaliser une feuille frontale (12) transparente et flexible ;
- à réaliser une feuille arrière flexible (14), imperméable à la vapeur ;
- à sceller ensemble les feuilles frontale et arrière (12, 14) au niveau d'un bord périphérique commun (16) où la surface de la feuille frontale (12) adjacente à la feuille arrière (14) comprend un mélange d'élastomère et de polymère thermoplastiques, la surface de la feuille arrière (14) adjacente à la feuille frontale (12), comprenant un polymère sélectionné dans le groupe se composant de polypropylène, de polyéthylène et un copolymère de polypropylène-polyéthylène ;
- à chauffer les feuilles frontale et arrière (12, 14) dans une première zone localisée pour fondre ensemble les parties chauffées des surfaces adjacentes, formant ainsi un premier joint décollable (24) s'étendant entre deux côtés du bord périphérique commun (16), ledit premier joint décollable joignant séparément les feuilles frontale et arrière, pour former ainsi un premier compartiment (18) pour contenir un diluant ;
- à chauffer les feuilles frontale et arrière dans une seconde zone localisée pour fondre ensemble les parties chauffées des surfaces adjacentes, formant ainsi un second joint décollable (26) s'étendant entre les deux côtés du bord périphérique commun (16), ledit second joint décollable (26)joignant séparément les feuilles frontale et arrière, pour former ainsi un compartiment de sortie (22) et un compartiment (20) pour contenir un médicament, le compartiment médicaments (20) étant placé entre le compartiment de sortie (22) et le compartiment diluant (18) ;
- à remplir le compartiment diluant (18) avec une solution à base de diluant et à remplir le compartiment médicaments (20) avec un médicament, tout en laissant vide le compartiment de sortie (22) ;
- à mettre en place une feuille (54) imperméable à l'humidité et ne laissant pas passer la lumière, et recouvrant le compartiment médicaments (20) où au moins une partie de la feuille (54) peut être enlevée pour le contrôle visuel du médicament dans le compartiment médicaments (20) ; où le premier joint décollable (24) peut être rompu par pression hydraulique
  générée par manipulation du compartiment diluant (18) et où, après rupture du premier joint décollable (24), le diluant et le médicament sont mélangés ensemble par une autre manipulation du récipient, pour former une solution diluant/médicament, après quoi le second joint décollable (26) peut être rompu par pression hydraulique générée par une autre manipulation des compartiments diluant et médicaments à présent joints, de sorte que la solution diluant/médicament peut s'écouler dans le compartiment de sortie (22) ; et
- à former un orifice de sortie (30) communiquant avec le compartiment de sortie (22) ; l'orifice de sortie (30) étant adapté pour être relié à un dispositif d'administration par voie intraveineuse.

15. Procédé selon la revendication 14, comprenant le chauffage des feuilles frontale et arrière (12, 14), en utilisant un appareil de thermocollage à double barre chaude ayant une barre frontale et une barre arrière, où la température de la barre frontale est supérieure à la température de la barre arrière.

16. Récipient flexible comme défini dans l'une quelconque des revendications 1 à 13, dans lequel l'orifice de sortie (30) s'engage dans la feuille frontale (12) et qui comprend une partie (38) formant le corps relié à une ouverture (32) de la feuille frontale (12) et qui s'étend transversalement par rapport au plan de la feuille frontale (12), où la feuille arrière (14) peut se plier contre la feuille frontale (12) lorsque le récipient est vidé.

17. Procédé comme défini dans l'une quelconque des revendications 14 à 16, dans lequel l'orifice de sortie (30) s'engage dans la feuille frontale (12) et qui comprend une partie (38) formant le corps relié à une ouverture (32) de

la feuille frontale (12) et s'étendant transversalement par rapport au plan de la feuille frontale (12), où la feuille arrière (14) est configurée pour se plier contre la feuille frontale (12) lorsque la solution diluant/médicament est vidée du récipient.

Fig. 1

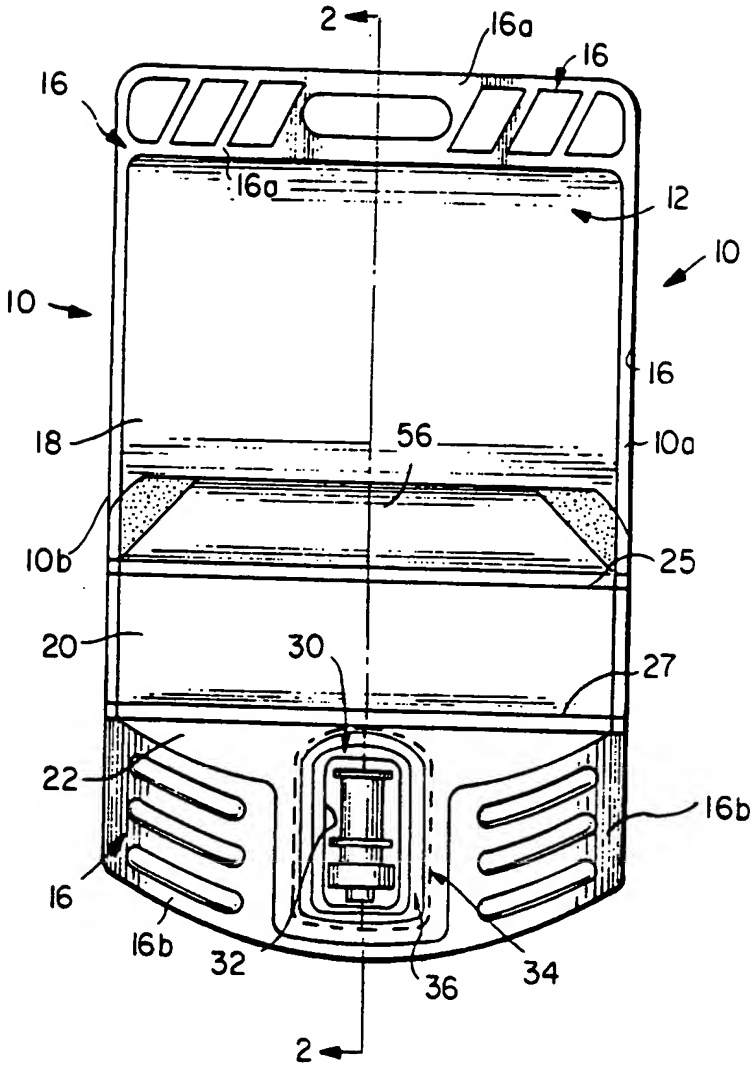
2
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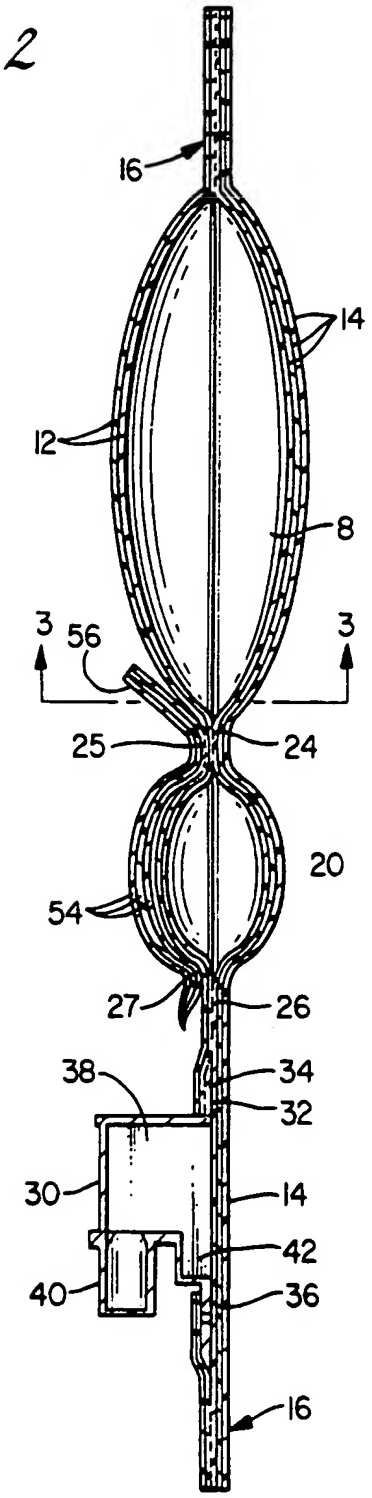
Fig. 2



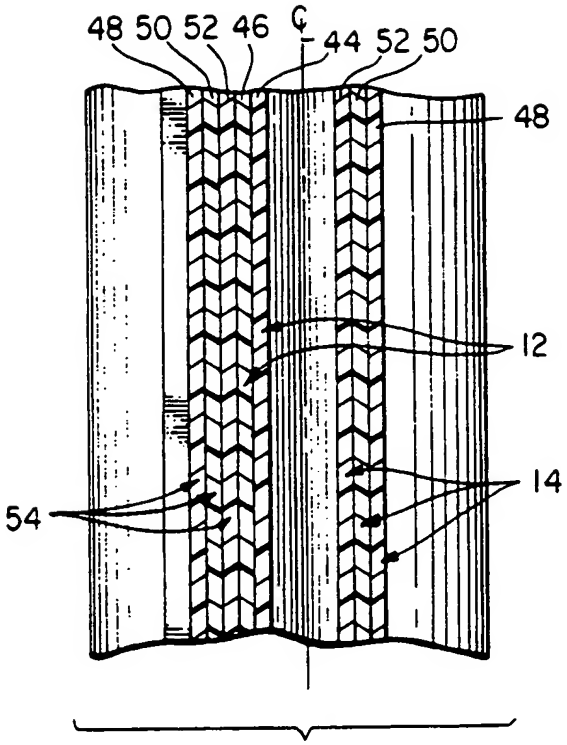


Fig. 3

Fig. 4

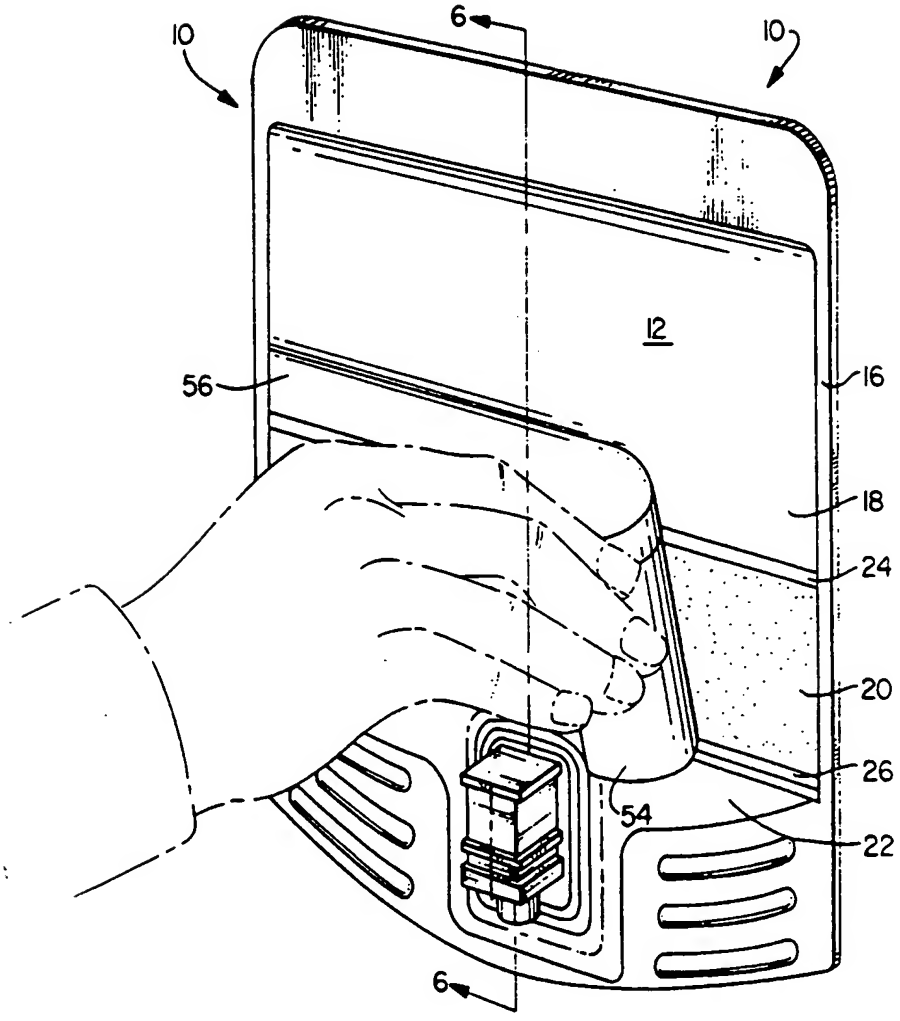


Fig. 5

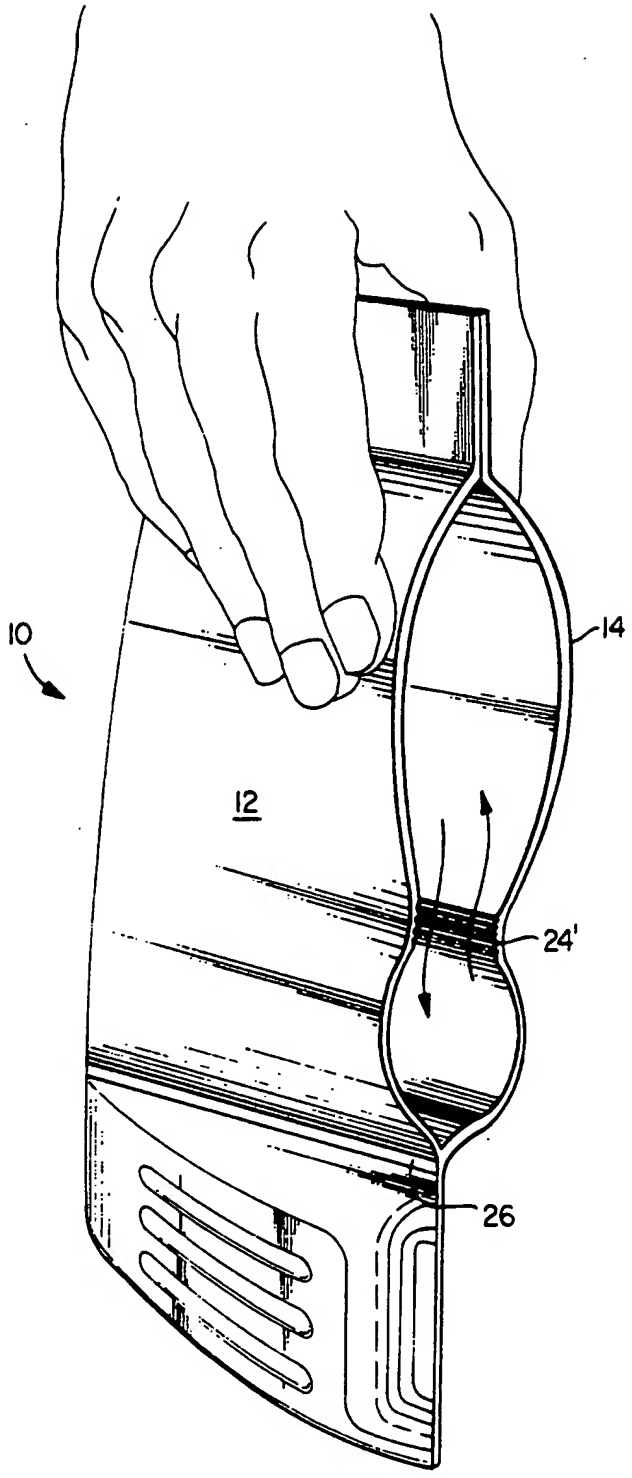


Fig. 6